

## CLAIMS

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A method of generating regulatory cells comprising:  
5 incubating one or more proteins comprising a cytolethal distending toxin (*cdt*), a leukotoxin (*ltx*) and/or a heat shock protein with blood cells for a time sufficient to induce differentiation, selective enrichment, and/or promoting proliferation of regulatory T cells.
2. The method of claim 1, wherein said proteins are secreted from at least  
10 one pathogenic organism.
3. The method of claim 2, wherein said pathogenic organism that secretes leukotoxin is *Actinobacillus actinomycetemcomitans*, *Mannheimia (Pasteurella) haemolytica*, or *Fusobacterium necrophorum*.
4. The method of claim 2, wherein said pathogenic organism that secretes a  
15 cytolethal distending toxin is *Actinobacillus actinomycetemcomitans*, *Escherichia coli*, *Shigella dysenteriae*, *Haemophilus ducreyi*, *Campylobacter upsaliensis*, *Campylobacter jejuni*, *Helicobacter hepaticus*, and *Salmonella enterica* serovar Typhi genome.
5. The method of claim 1, wherein said proteins are in a crude extract.
6. The method of claim 1, wherein said proteins are in a purified form.
- 20 7. The method of claim 1, wherein said proteins are expressed from at least one expression plasmid.
8. The method of claim 1, wherein said heat shock gene is GroEL.
9. The method of claim 1, wherein said blood cells are concentrated peripheral blood mononuclear cells.
- 25 10. The method of claim 1, wherein said regulatory T cells are Tr1.
11. A method of inducing differentiation and promoting proliferation of regulatory T cells comprising:  
incubating peripheral blood mononuclear cells in the presence of at least three  
proteins, cytolethal distending toxin (*cdt*), leukotoxin (*ltx*) and a heat shock protein; and  
30 selecting for Tr1 cells.

12. The method of claim 11, wherein said proteins are secreted from a pathogenic organism.

13. The method of claim 12, wherein said pathogenic organism is *Actinobacillus actinomycetemcomitans*.

5 14. The method of claim 11, wherein said proteins are introduced into said peripheral blood mononuclear cells in a purified form.

15. The method of claim 11, wherein said proteins are introduced into said peripheral blood mononuclear cells as a crude extract.

10 16. The method of claim 11, wherein said proteins are introduced into said peripheral blood mononuclear cells by way of an expression vector.

17. A composition comprising an expression vector comprising a coding sequence for a cytolethal distending toxin (*cdt*), a leukotoxin (*ltx*) and a heat shock protein.

18. The expression vector of claim 17, further comprising a liposome.

15 19. The expression vector of claim 18, for use as an immunosuppressant agent.

20. A method for suppressing the immune system of an individual having a disorder, comprising:

20 administering the regulatory cells produced from the method of claim 1, to an individual.

21. The method of claim 20, wherein said disorder is an autoimmune disease, an inflammatory disorder, and/or a rejection of a transplant.

25 22. The method of claim 21, wherein said autoimmune disease is allergies, inflammatory myopathy, Myasthenia Gravis, inflammatory polyneuropathies, Multiple Sclerosis, asthma, insulin-dependent diabetes mellitus (IDDM), autoimmune thyroiditis, autoimmune gastritis accompanying pernicious anemia, psoriasis, uveitis, rheumatoid arthritis, Systemic lupus erythematosus (SLE) and/or colitis.

23. The method of claim 21, wherein said transplant is a solid organ transplant.

30 24. The method of claim 23, wherein said solid organ is a kidney, heart, lung, liver, and/ or pancreas.

25. The method of claim 21 wherein transplant is a cell.
26. The method of claim 25, wherein said cell is bone marrow, stem cell, and /or a pancreatic islet.
27. The method of claim 26, wherein said transpant is a tissue.
- 5 28. The method of claim 27, wherein said tissue is corneal, lens, and/or skin.
29. The method of claim 21 wherein said inflammatory disease is an inflammatory bowl disorder (IBD), asthma, allergic and atopic reactions.
30. A method of suppressing the immune system in a mammal comprising, contacting peripheral blood cells with at least one toxin that induces differentiation and promotes proliferation of regulatory T cells having the marker CD4<sup>+</sup> CD25<sup>+</sup> and express interleukin-10; isolating the regulatory T cells and administering to the mammal a composition enriched for regulatory T cells.
- 10 31. The method of claim 30, wherein said administration occurs by, intravenous, intraperitoneal, subcutaneous, intradermal, intranodal, intramuscular, transdermal, inhaled, intranasal, rectal, vaginal, urethral, topical, oral, intraocular, intraarticular, intracranial, and/or intraspinal or any combination thereof.
- 15 32. An immunosuppressive agent comprising an organism carrying an expression vector capable of expressing a cytolethal distending toxin (*cdt*), a leukotoxin (*ltx*) and a heat shock protein.
- 20 33. A method of suppressing the immune system of a mammal, comprising: administering to said mammal an attenuated strain of *Actinobacillus actinomycescomitans*, wherein said attenuated strain is incapable of causing disease and fully expresses a cytolethal distending toxin (*cdt*), a leukotoxin (*ltx*) and a heat shock protein.

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